West Virginia Bureau for Public Health
Your Health Your Safety Our Purpose
Department of Health & Human Resources

Spotted Fever Rickettsiosis,

Including Rocky Mountain spotted fever (RMSF)

Surveillance Protocol

Note: In 2010, the CDC changed the disease event name from "Rocky Mountain Spotted Fever" to "Spotted Fever Rickettsiosis". The CDC RMSF Supplemental Form should be used to report information of all Spotted Fever Rickettsiosis, including Rocky Mountain spotted fever.

Rocky Mountain spotted fever (RMSF) is a tickborne infectious disease that is most commonly associated with the bite of the American dog tick, *Dermacentor variabilis* (on the eastern and southern United States; other tick species are important vectors of RMSF in the western part of the United States)[1]. RMSF is classified as a tickborne rickettsial disease (TBRD), which encompasses other related conditions including ehrlichiosis and anaplasmosis. RMSF is the most commonly reported fatal tickborne disease, with a case-fatality rate as high as 30% if left untreated[2,3,4]. RMSF is of public health importance due to presence of the primary tick vector in West Virginia, the high case-fatality rate among untreated cases, the preventability of infection, and the need to monitor the descriptive epidemiology of reported RMSF cases.

Provider Responsibilities

1. Report suspect, probable and confirmed cases of spotted fever ricketsioses (including RMSF) to the local health department within one week of diagnosis. Include copies of all laboratory reports (including CBC and metabolic panels).

2. Free IFA serology testing is available for clinically appropriate specimens. To participate in this program:
    a. First, call DIDE at 1-800-423-1271 to request approval for RMSF testing. A DIDE epi-on-call will complete the form over the phone with the provider (prior approval is required before sending a specimen)
        i. Approval is based on whether the patient illness is clinically compatible with RMSF, which means presence of a **fever** and at least one of the following:
            1. Rash; or
            2. Eschar; or
            3. Headache; or
            4. Myalgia; or
            5. Anemia; or
            6. Thrombocytopenia; or
            7. Elevated hepatic transaminase levels

        ii. Note: If RMSF infection is suspected, do not wait for serologic test results before initiating recommended antibiotic treatment

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iii. Specimen collection timing is critical*, as most patients lack diagnostic antibody levels during the first week of clinical illness. Paired sera (2-3 weeks apart) are required for confirmation of diagnosis; single positive specimens are presumptive evidence of infection. Please note the following:
   1. **Specimens collected prior to day 7 of illness** will be frozen and held until a convalescent serum specimen is received (must be received within 45 days). Once received, both specimens will be paired, tested and a result will be reported. If no convalescent is specimen is received, no testing will be performed.
   2. **Specimens collected on day 7 of illness or later** will be tested when received and a result will be reported, regardless of receipt of a convalescent specimen. An aliquot of the original specimen will be stored frozen for 45 days, which will be tested alongside a convalescent specimen, if received. If received, the result from the paired specimen testing will also be reported.

b. After approval, collect specimen in a red top tube; serum must be sent refrigerated or frozen (do not thaw) and the completed form must be included with the specimen
c. Specimens should be sent to the following address:

Virology Laboratory – CAMC Memorial
Attention: Linda Minnich
3200 MacCorkle Avenue
Charleston WV 25304
Phone – 304-388-4308 or 9618.

d. Specimen results will be sent to the submitter based on the timing of specimen collection relative to onset date, as outlined in section 2.b.ii.
e. A convalescent specimen reminder will be sent to the submitter 2 weeks after receipt of the acute specimen. For convalescent specimens, DIDE should be contacted to update the serology form to accompany specimen.

**Note: patients with RMSF do not generally develop detectable levels of antibodies until the second week of illness. CDC recommends two serum specimens collected 2-3 weeks apart and tested using indirect immunofluorescence assay (IFA) to confirm diagnosis[1]. IFA is considered the gold standard for serological testing of RMSF specimens. A CBC with metabolic panel is useful in the interim to guide differential diagnosis and treatment decisions[1].*

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Laboratory Responsibilities

1. Report positive test results for spotted fever rickettsioses to the local health department within 1 week.

Public Health Action

1. When a case is reported:
    a. Enter the case into WVEDSS
    b. Contact the healthcare provider to document/determine the following:
        i. Record symptom onset date
        ii. Clinical symptoms of fever, headache, myalgia, anemia, thrombocytopenia, leukopenia, elevated hepatic transaminases or others
        iii. Document underlying immunosuppressive condition(s)
        iv. Document any life-threatening complications of the illness
        v. Examine the laboratory testing that was done to ensure all testing that was performed on the case has been reported to DIDE
        vi. Collect case's demographic data and contact information (birth date, county, sex, race/ethnicity, occupation, address, phone number(s))
        vii. Record hospitalizations: location, admission and discharge dates
        viii. Record outcomes: recovered or date of death

    c. Interview the case or proxy to determine source and risk factors; focus on the 2-week incubation period prior to illness onset.
        i. Document recent travel to endemic areas or history of possible exposure to ticks. List geographic location(s) and date(s). Consider:
            1. Exposure to animals or pets with ticks
            2. Outdoor activities
            3. Occupational risks (e.g., laboratory worker, landscape worker, etc.)
        ii. Determine case's history of tick bites, include geographic location of bite and date

    d. Complete the supplemental CDC form ("Tick-borne Rickettsial Disease Case Report") within 30 days of the original case report date

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e. Fax or mail copies of all appropriate laboratory reports and the CDC supplemental form to the Division of Infectious Disease Epidemiology within 45 days of the original case report date

2. Educate providers and laboratories to report cases of RMSF to the local health department in the patient's county of residence within one week of diagnosis.

3. Educate healthcare providers to:
   a. Consider the likely exposures to tick habitats when assessing patients with suspected RMSF.
   b. Recognize the importance of early treatment for suspected RMSF cases. Do not wait for laboratory confirmation, or rely on the presence of "classic" RMSF symptoms (e.g., most patients will seek care 1-2 days before the rash develops, and rash may be absent in up to 20% of patients[1]) before beginning proper antibiotic therapy; history of tick bite can also be misleading (approximately 40% of RMSF cases report no history of tick bite[1])
   c. Order appropriate laboratory testing for RMSF based on the timing of symptom onset. Most patients seek care during the first week of illness, well before detectable levels of antibody are generated[1]. CDC recommends two serum specimens collected 2 - 3 weeks apart (starting on week 2 of illness) and tested using indirect immunofluorescence assay (IFA) to confirm diagnosis[1]. A CBC with metabolic panel is useful in the interim to guide differential diagnosis and treatment decisions[1].

4. Educate veterinarians to report possible household clusters of RMSF in pets and their owners to the local health department[1,6,7].

5. Educate the public about tickborne disease prevention. See http://www.cdc.gov/ticks/avoid/index.html

Disease Control Objectives

1. Reduce the risk of severe disease and death through educating physicians in early recognition, diagnosis and treatment of RMSF.

Disease Prevention Objectives

1. Reduce the risk of disease during tick season by educating the public to:
   a. Use personal protective measures when visiting tick habitats
   b. Keep pets free of ticks

c. Perform tick checks following visits to tick habitats
d. Promptly and correctly remove ticks found on the body

Disease Surveillance Objectives

1. To monitor incidence of RMSF in West Virginia and perform descriptive epidemiology on reported cases
2. Determine if reported cases are being provided with appropriate and timely antibiotic treatment

Public Health Significance

RMSF is a nationally notifiable condition that has been a reportable disease in the United States since the 1920s[11]. RMSF is the most commonly reported fatal tickborne disease in the United States and fatal cases have been documented in West Virginia[5]. Incidence is highest among children <10 years, and case-fatality rates are disproportionately higher among children <5 years compared with other age groups. With early recognition and antibiotic treatment, clinical severity is markedly reduced. Additionally, several prevention mechanisms are available to the public to reduce tick exposures. The principal vector in West Virginia is *Dermacentor variablis*, the dog tick. Surveys carried out in two neighboring states (Kentucky and Maryland) estimate the spotted fever group infection rate of *D. variablis* ticks to be 6.0%[10].

Clinical Description

Illness is characterized by acute onset of fever, and may be accompanied by headache, malaise, myalgia, nausea/vomiting, or neurologic signs; a macular or maculopapular rash appears 4-7 days following onset in many (~80%) patients, often present on the palms and soles. RMSF may be fatal in as many as 20% of untreated cases, and severe, fulminant disease can occur. The presence of an eschar at the site of tick attachment has been reported for some other spotted fever rickettsioses which usually present with clinical presentation that appears similar to, but may be milder than, RMSF.

Etiologic Agent

Rickettsia species of the Spotted Fever group (obligate intracellular coccobacillus): *R. rickettsii*, *R. parkeri* and *R. phillipi* (proposed).

Reservoir

Rickettsial organisms are able to maintain themselves in ticks (primarily *D. variablis* in West Virginia) in the environment through transovarial and transstadial transmission[8].

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Other important tick vectors identified in the United States include *D. andersonii* (Rocky Mountain wood tick), *Rhiphicephalus sanguineus* (brown dog tick) and *Amblyomma maculatum* (Gulf Coast tick). The *Rickettsia* spp. life cycle is complex and includes small mammals as well as birds; humans are not part of the natural life cycle.

Mode of Transmission

The mode of transmission for RMSF is through the bite of an infected tick. An infected tick must be attached for approximately 4 - 6 hours of tick to infect a human. Fluids from infected ticks that have been crushed can also cause infection through breaks in the skin. Transfusion-associated transmission has been documented but is rare.

Incubation Period

The incubation period of RMSF ranges from 3 to 14 days (typically, one week).

Period of Communicability

There is no person-to-person transmission of RMSF. Ticks remain infected for life, which is normally around 18 months.

Outbreak Recognition

Outbreaks of RMSF are rare but have been documented in other states. In addition, clusters of RMSF have been reported among household members as well as among pets and pet owners[3,4,6,7].

Case Definition

(The following section is from CDC—read information below in the case classification section regarding clinical and laboratory evidence necessary to classify cases)[9]

Clinical Description

Spotted fever rickettsioses are a group of tickborne infections caused by some members of the genus *Rickettsia*. Rocky Mountain spotted fever (RMSF) is an illness caused by *Rickettsia rickettsii*, a bacterial pathogen transmitted to humans through contact with ticks. *Dermacentor* species of ticks are most commonly associated with infection, including *Dermacentor variabilis* (the American dog tick), *Dermacentor andersoni* (the Rocky Mountain wood tick), and more recently *Rhiphicephalus sanguineus* (the brown dog tick). Disease onset averages one week following a tick bite. Age-specific illness is highest for children and older adults. Illness is characterized by acute onset of fever, and may be accompanied by headache, malaise, myalgia, nausea/vomiting, or neurologic

signs; a macular or maculopapular rash appears 4-7 days following onset in many (~80%) patients, often present on the palms and soles. RMSF may be fatal in as many as 20% of untreated cases, and severe, fulminant disease can occur. In addition to RMSF, human illness associated with other spotted fever group Rickettsia species, including infection with *Rickettsia parkeri* (associated with Amblyomma maculatum ticks), has also been reported. In these patients, clinical presentation appears similar to, but may be milder than, RMSF; the presence of an eschar at the site of tick attachment has been reported for some other spotted fever rickettsioses.

Clinical evidence
Any reported fever and one or more of the following: rash, eschar, headache, myalgia, anemia, thrombocytopenia, or any hepatic transaminase elevation.

Laboratory criteria for diagnosis
The organism in the acute phase of illness is best detected by polymerase chain reaction (PCR) and immunohistochemical methods (IHC) in skin biopsy specimens, and occasionally by PCR in appropriate whole blood specimens taken during the first week of illness, prior to antibiotic treatment. Serology can also be employed for detection, however an antibody response may not be detectable in initial samples, and paired acute and convalescent samples are essential for confirmation.

For the purposes of surveillance,

Laboratory confirmed:

i. Serological evidence of a fourfold change in immunoglobulin G (IgG)-specific antibody titer reactive with Rickettsia rickettsii or other spotted fever group antigen by indirect immunofluorescence assay (IFA) between paired serum specimens (one taken in the first week of illness and a second 2-4 weeks later), or
ii. Detection of R. rickettsii or other spotted fever group DNA in a clinical specimen via amplification of a specific target by PCR assay, or
iii. Demonstration of spotted fever group antigen in a biopsy or autopsy specimen by IHC, or
iv. Isolation of R. rickettsii or other spotted fever group rickettsia from a clinical specimen in cell culture.

Laboratory supportive:

v. Has serologic evidence of elevated IgG or IgM antibody reactive with R. rickettsii or other spotted fever group antigen by IFA, enzyme-linked immunosorbent assay (ELISA), dot-ELISA, or latex agglutination.

Note: Current commercially available ELISA tests are not quantitative, cannot be used to evaluate changes in antibody titer, and hence are not useful for serological confirmation. IgM tests are not strongly supported for use in serodiagnosis of acute disease, as the response may not be specific for the agent (resulting in false positives) and the IgM response may be persistent. Complement fixation (CF) tests and other older test methods are neither readily available nor commonly used. CDC uses in-house IFA IgG testing (cutoff of ≥1:64), preferring simultaneous testing of paired specimens, and does not use IgM results for routine diagnostic testing.

Exposure
Exposure is defined as having been in potential tick habitats within the past 14 days before onset of symptoms. Occupation should be recorded if relevant to exposure. A history of a tick bite is not required.

Case Classification
Suspected: A case with laboratory evidence of past or present infection but no clinical information available (e.g. a laboratory report).

Probable: A clinically compatible case (meets clinical evidence criteria) that has supportive laboratory results.

Confirmed: A clinically compatible case (meets clinical evidence criteria) that is laboratory confirmed.

Preventive Interventions
See "Disease Prevention Objectives" section.

Treatment
Doxycycline is the treatment of choice. Chloramphenicol is an alternative when contraindications to tetracyclines exist (e.g., child < 8 years of age, pregnancy).

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Appropriate antibiotic treatment should be initiated immediately when there is a suspicion of a tickborne rickettsial disease (TBRD). Treatment should not be delayed until laboratory confirmation is obtained.

Surveillance Indicators

1. Proportion of probable or confirmed cases where the case was completed and submitted to DIDE within 30 days of initial report date
2. Proportion of probable or confirmed cases with onset date complete
3. Proportion of probable or confirmed cases with county of residence complete
4. Proportion of probable or confirmed cases with travel history documented

References

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